FIGURE 1A

CTCGAGGACAGTGACCTGGGAGTGAGTACAAGGTGAGGCCACCACTCAGGGT
GCCAGCTCCAAGCGGGTCACAGGGACGAGGGCTGCGGCCATCAGGAGGCCCT
GCACACACATCTGGGACACGCGCCCCCGAGGGCCAGTTCACCTCAGTGCGCCT
CATTCTCCTGCACAAAAGCGCCCCCATCCTTTCTTCACAAGGCTTTCGTGGAAG
CAGAGGCGTCGATGCCCAGTACCCTCTCCCTTTCCCAGGCAACGGGACCCCAA
GTTTGCTGACTGGGACCACCAAGCCACGCATGCGTCAAGAGTGAGAGTCCGG
GACCTAGGCAGGGGCCCTGGGGTTGGGCCTGAGAGAGAAGAGAACCTCCCCC
AGCACTCGGTGTGCATCGGTAGTGAAGGAGCCTCACCTGACCCCCGCTGTTGC
TCAATCGACTTCCCAAGAACAGAGAGAAAAGGGAACTTCCAGGGCGGCCCGG
GCCTCCTGGGGGTTCCCACCCCATTTTTAGCTGAAAGCACTGAGGCAGAGCTC
CCCCTACCCAGGCTCCACTGCCCGGCACAGAAATAACAACCACGGTTACTGAT
CATCTGGGAGCTGTCCAGGAATTC

EP 2 360 265 A1 20110824

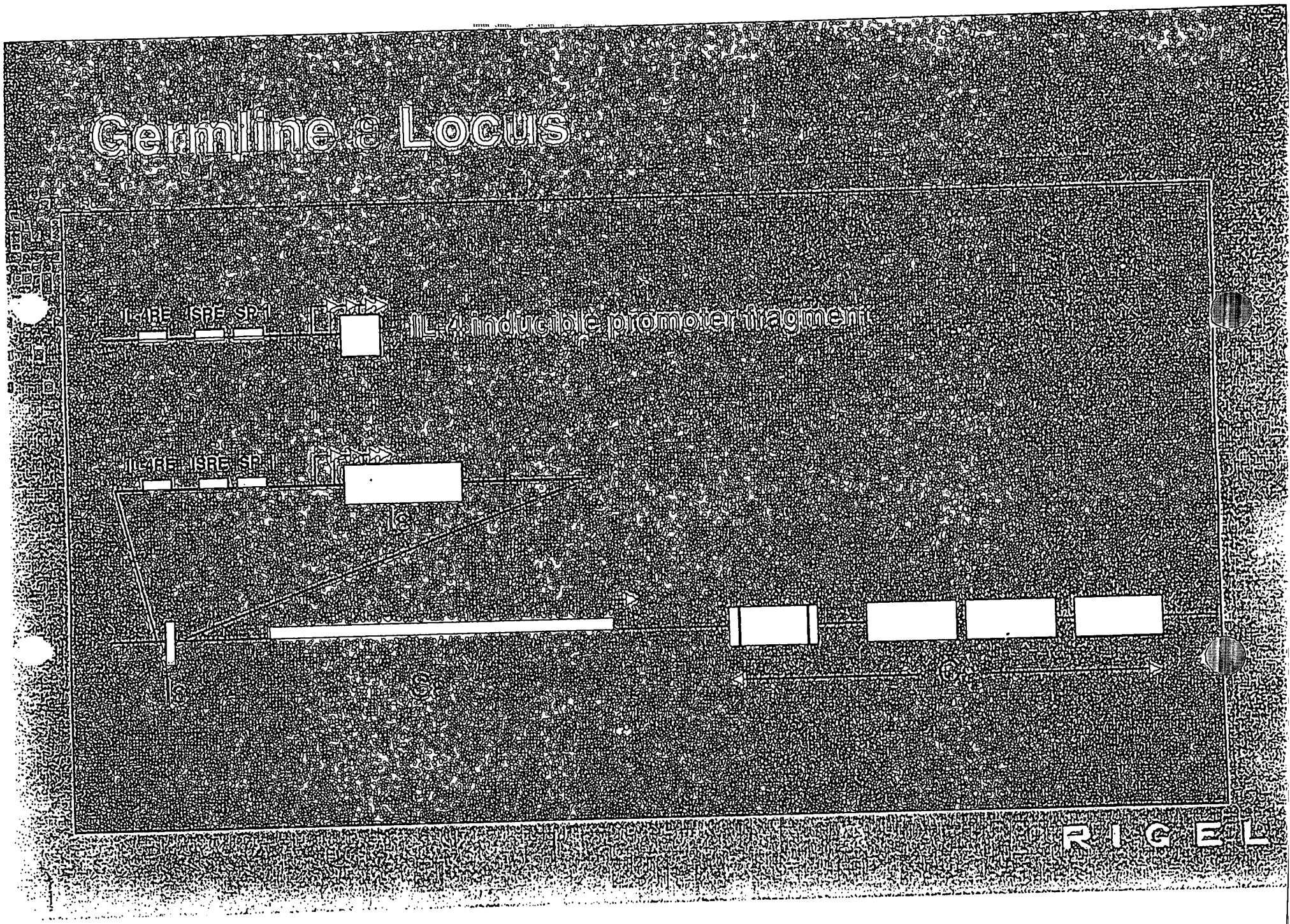

Germline ε Locus
IL-4 inducible promoter fragment
IL4RE ISRE SP-1
IL4RE ISRE SP-1
1B
1A
1C
RIGEL

FIGURE 1B

Low energy DNA folding of the Sε region

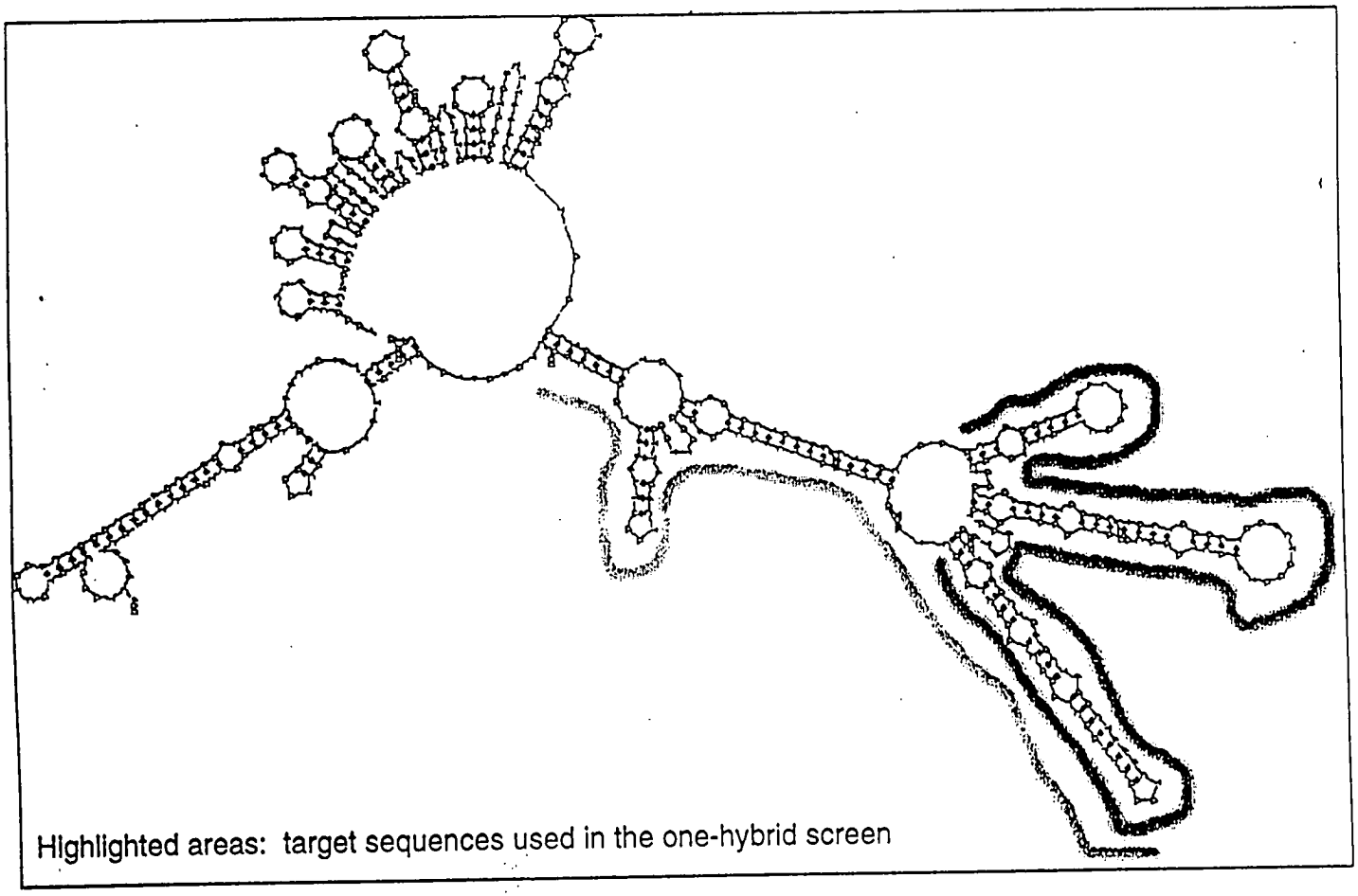


FIG 2A

Appendix E

FIGURE 2B

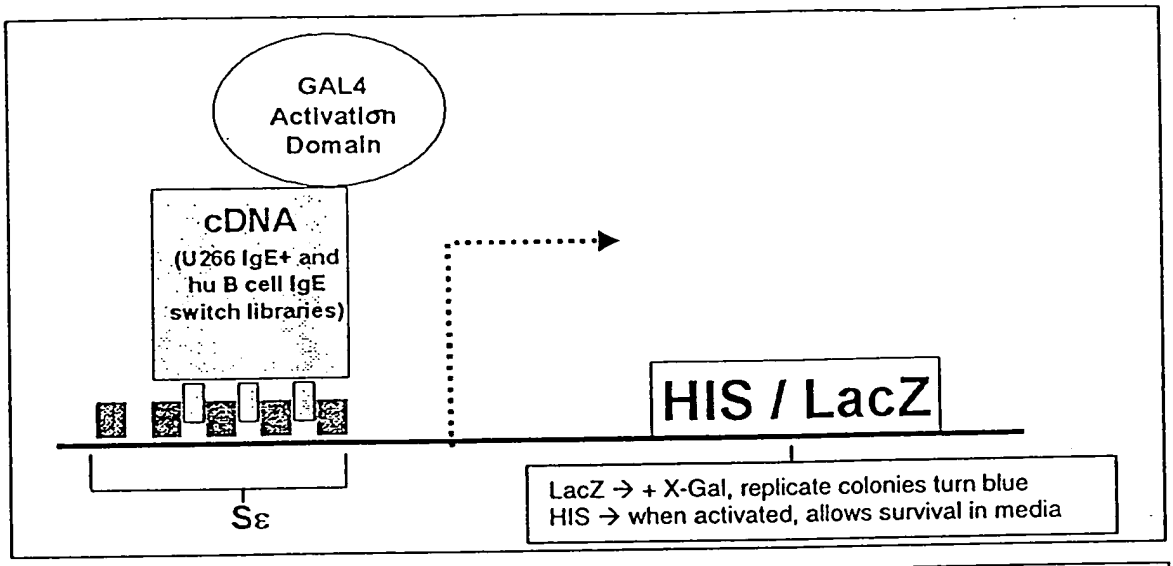
```
  1  GCTGGGCTAA ACTGGGCTAG CCTGAGCTGG GCTGAACTGG GCTGCTGGGC
 51  TGGACTGGGT AAGCTGGGCT GAGCTGGGTT GGGTGGAAAT GGGCTGAGCT
101  GAGCTAGGCT AAACTGGGTT TGGCTGGGCT GGGCTGGGCT GGG
```

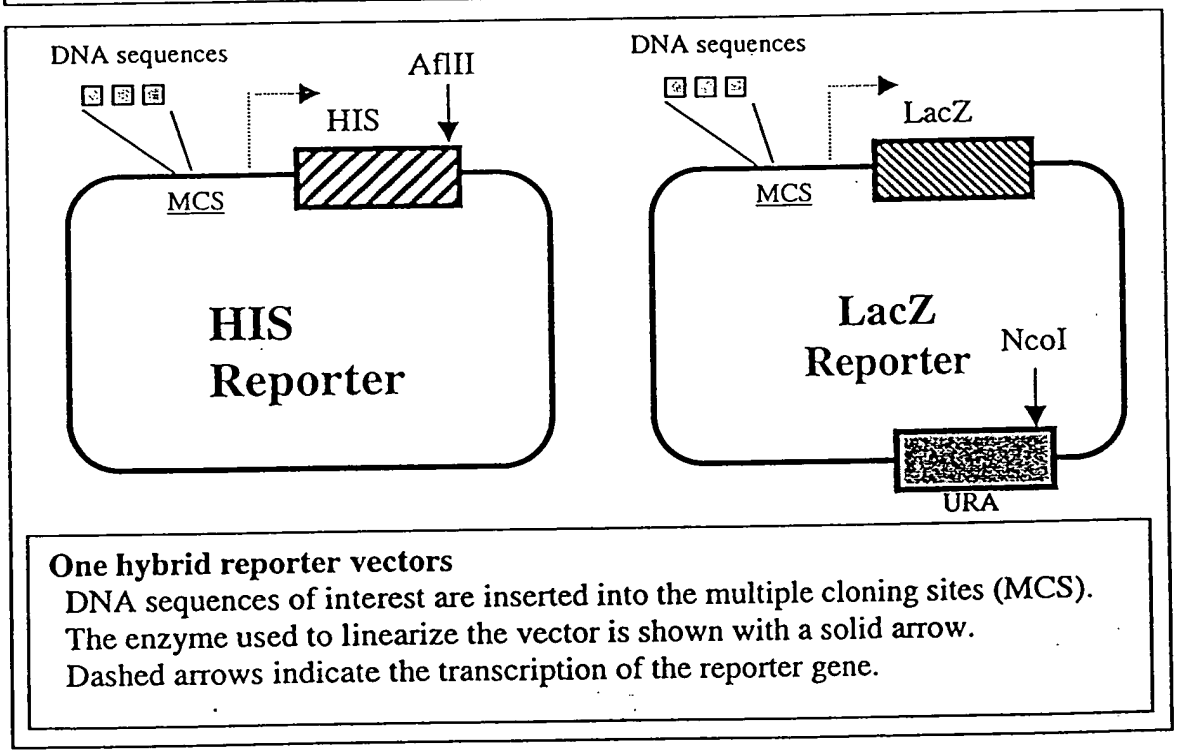
FIGURE 2C

```
  1  GGTTTGGCTG GGCTGGGCTG GGCTGGGCTG GGTTCAGCTG AGCGGGTTGG
 51  GTTAGACTGG GTCAAACTGG TTCAGC
```

FIG 3

Appendix F Yeast One-Hybrid Screening





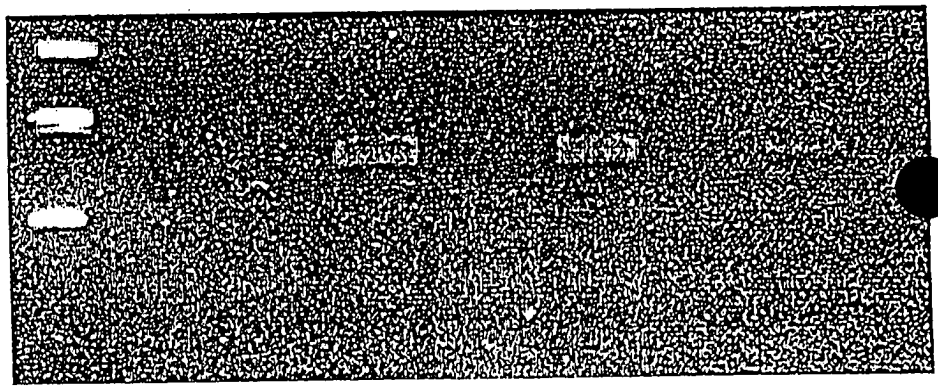
One hybrid reporter vectors
DNA sequences of interest are inserted into the multiple cloning sites (MCS).
The enzyme used to linearize the vector is shown with a solid arrow.
Dashed arrows indicate the transcription of the reporter gene.

Docket No. 2000-0056

FIG 4

IL-4 Induction of Germline ε mRNA in the IgM+ B cell lines: CA-46, MC-116 and DND39

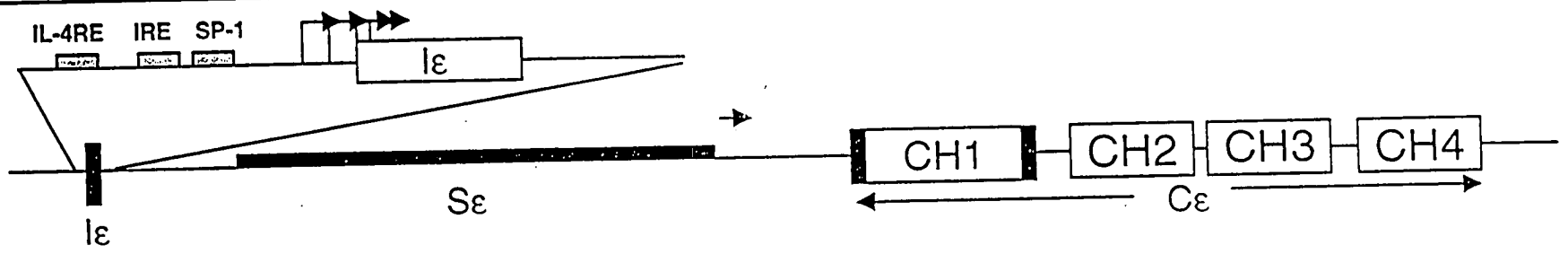
Cells were incubated for 48 hrs in 300 U/ml of h-IL-4. RT-PCR was performed using primers specific for the germline ε exon and the 5'-end of the ε CH1 exon (predicted size ~ 200 bp).



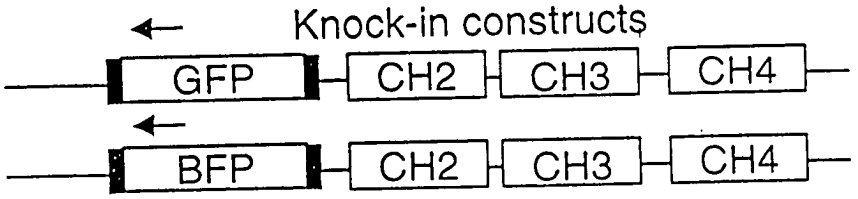
Appendix G

FIG. 5

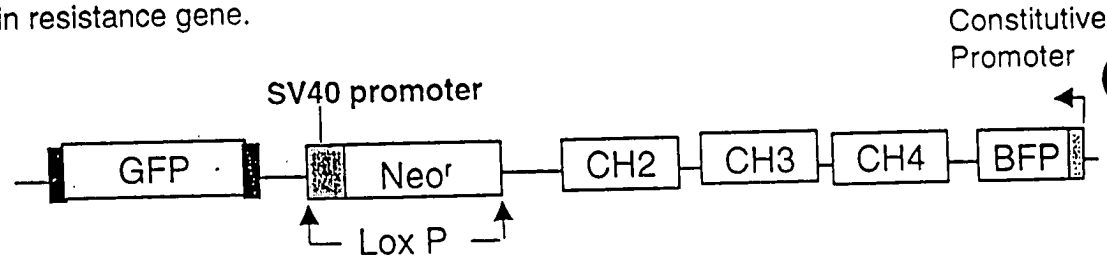
Approaches to generate germline ε promoter knock-in reporter cell lines



IL-4 inducible IgM+ B cell lines are transfected. Under the influence of IL-4, GFP and/or BFP positive clones are isolated by FACS. Homologous recombination can be confirmed by PCR and/or Southern blot hybridization.



IL-4 inducible IgM+ B cell lines are transfected and selected with G418. Survivors are sorted for the lack of 3' BFP expression (deleted during homologous recombination). RT-PCR is performed to confirm homologous recombination. Those clones are transfected with *cre* to remove the neomycin resistance gene.



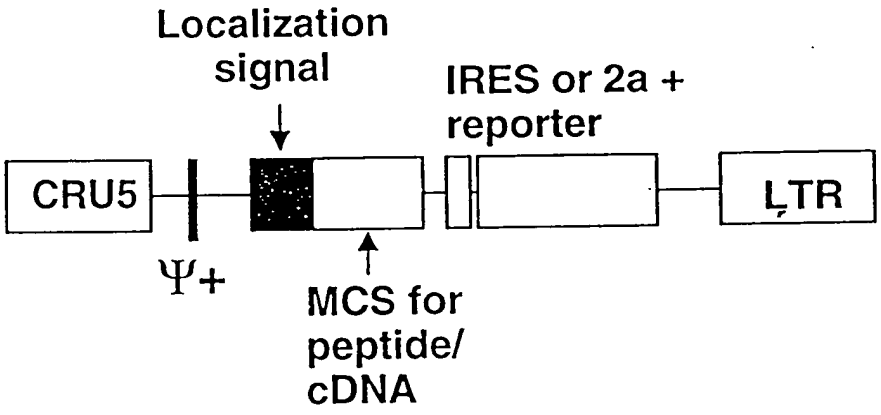
Il-4 RE, IL-4 responsive element
IRE, interferon responsive element
SP-1, SP-1 binding site
Iε, non-translated exon
Sε, switch region of ε
GFP, green fluorescent protein
BFP, blue fluorescent protein
CH1,2,3,4, constant region domain exons

Appendix A

FIG 6

Appendix I

Rigel Base Vector



All components are cassetted for flexibility

CRU5, modified LTR
LTR, long terminal repeat
ψ+, packaging signal
Localization signal: nuclear, cell membrane, granular
MCS, multiple cloning site
IRES, internal ribosome entry site
2a, self-cleaving peptide

Rigel 00000000

FIG 7

Appendix H

Protocol for Transfection of Phoenix Cells and Infection of Nonadherent Target Cells

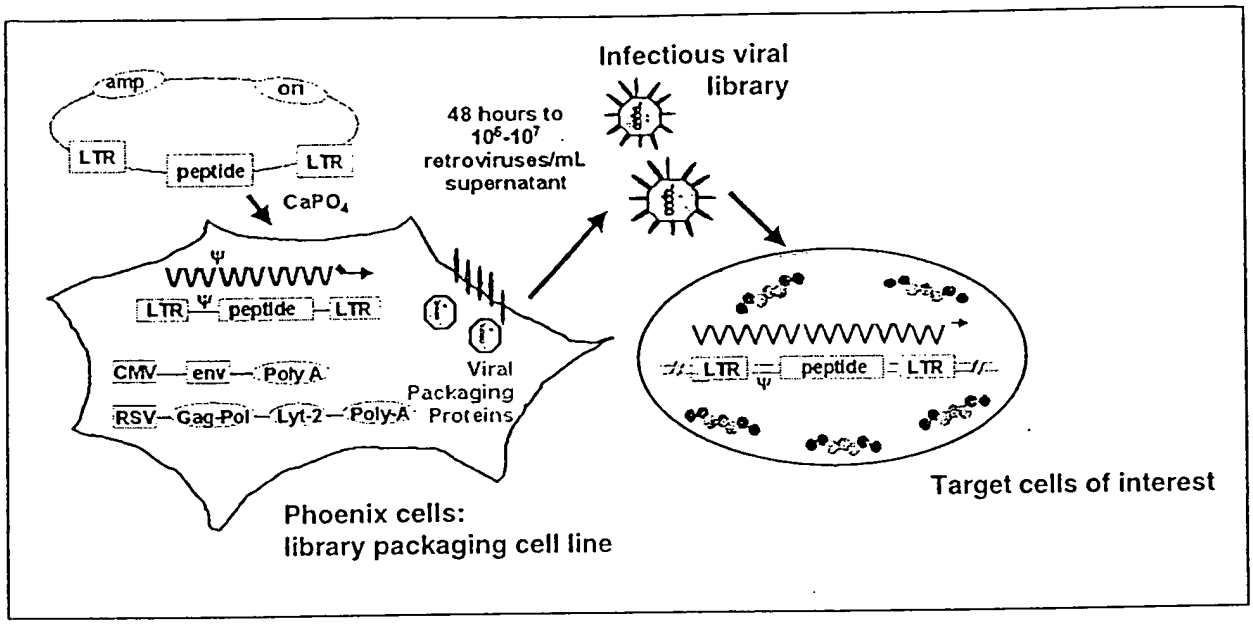
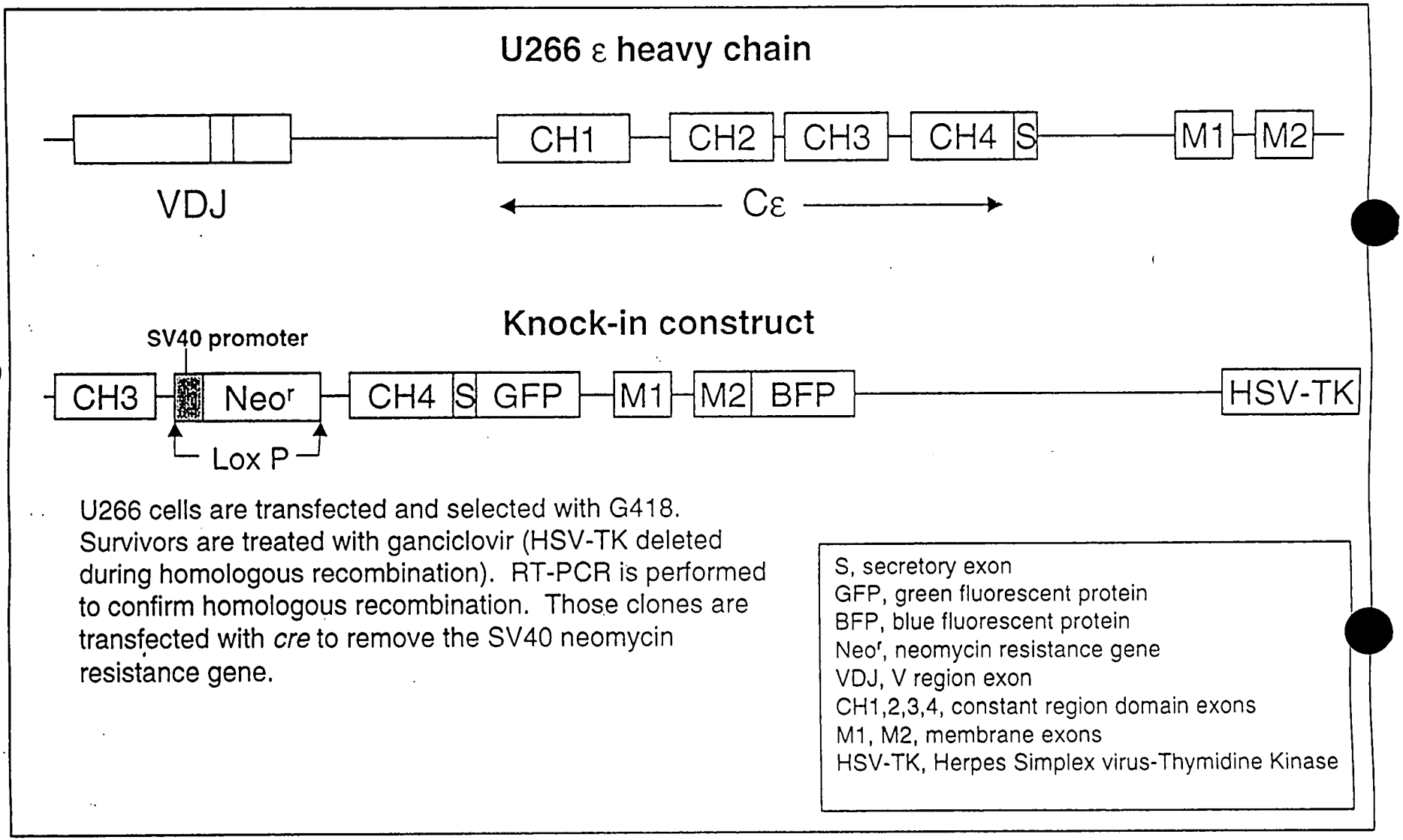


FIG 8

Rigel, Inc.
Confidential

ε heavy chain GFP/BFP knock-in cell line



U266 cells are transfected and selected with G418. Survivors are treated with ganciclovir (HSV-TK deleted during homologous recombination). RT-PCR is performed to confirm homologous recombination. Those clones are transfected with *cre* to remove the SV40 neomycin resistance gene.

S, secretory exon
GFP, green fluorescent protein
BFP, blue fluorescent protein
Neor, neomycin resistance gene
VDJ, V region exon
CH1,2,3,4, constant region domain exons
M1, M2, membrane exons
HSV-TK, Herpes Simplex virus-Thymidine Kinase

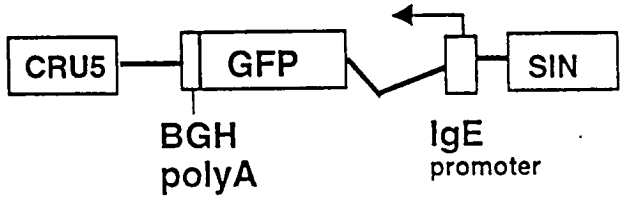
Appendix D

TOZ260-S2F5669

A

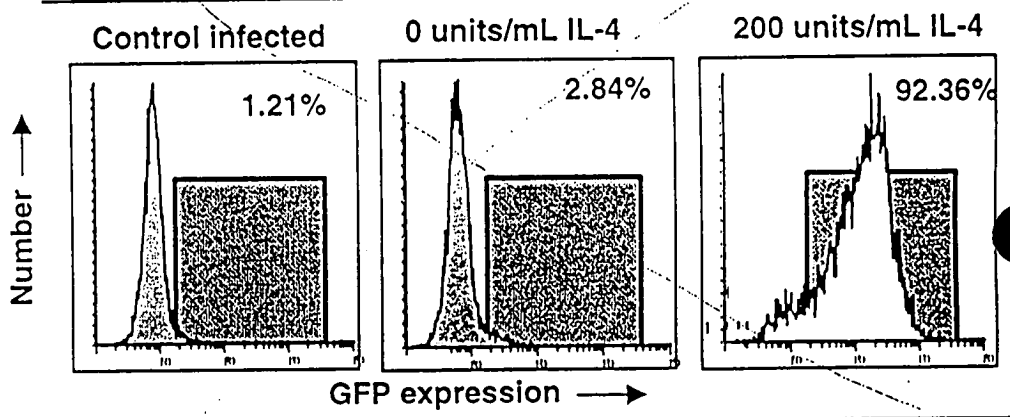
IL-4 Inducible ε Promoter Reporter Cell Line

Reporter construct



CRU5, hCMV promoter plus R and U5 regions of LTR
GFP, green fluorescent protein
BGH poly A, bovine growth hormone poly-adenylation signal
SIN, self-inactivating LTR

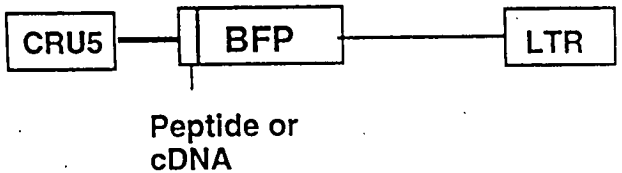
IL-4 induced reporter



B

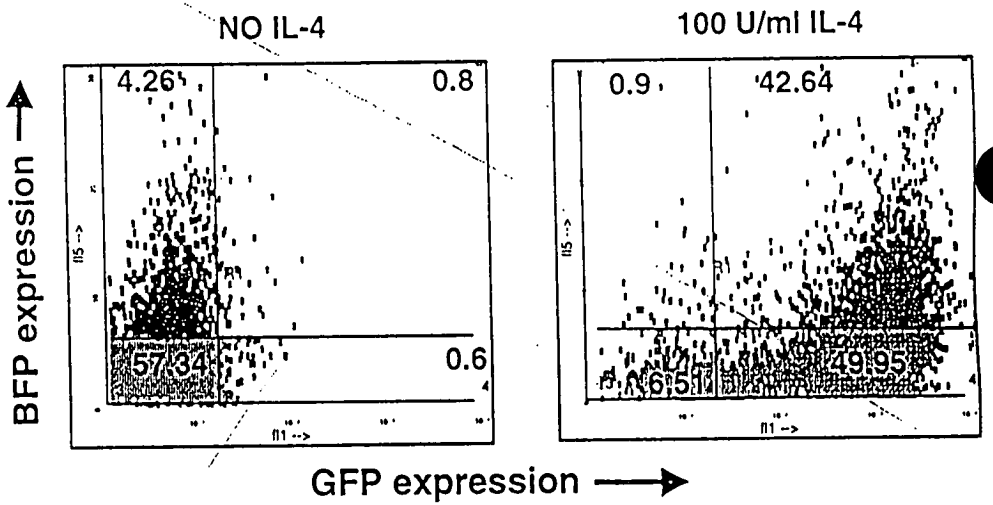
Reporter Line Infected with BFP Construct

Library construct



BFP, blue fluorescent protein

FACS profile of cells with both reporter and peptide library



Appendix C

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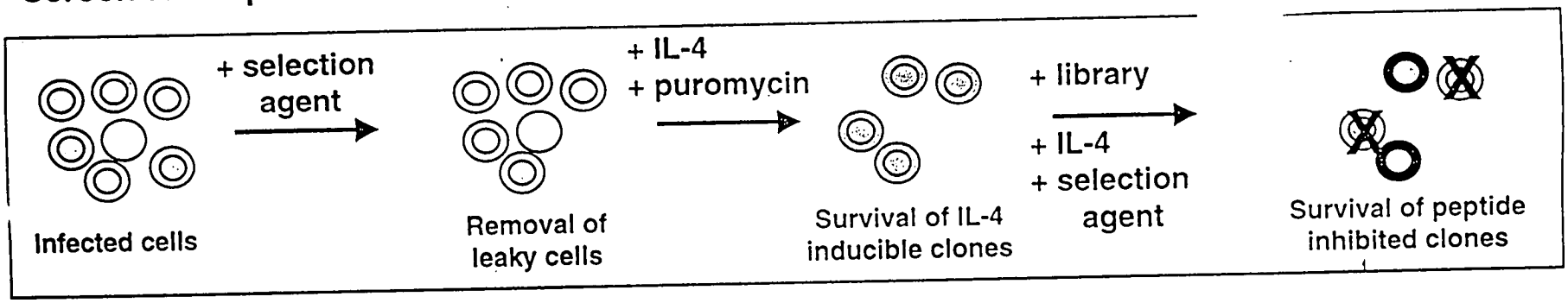
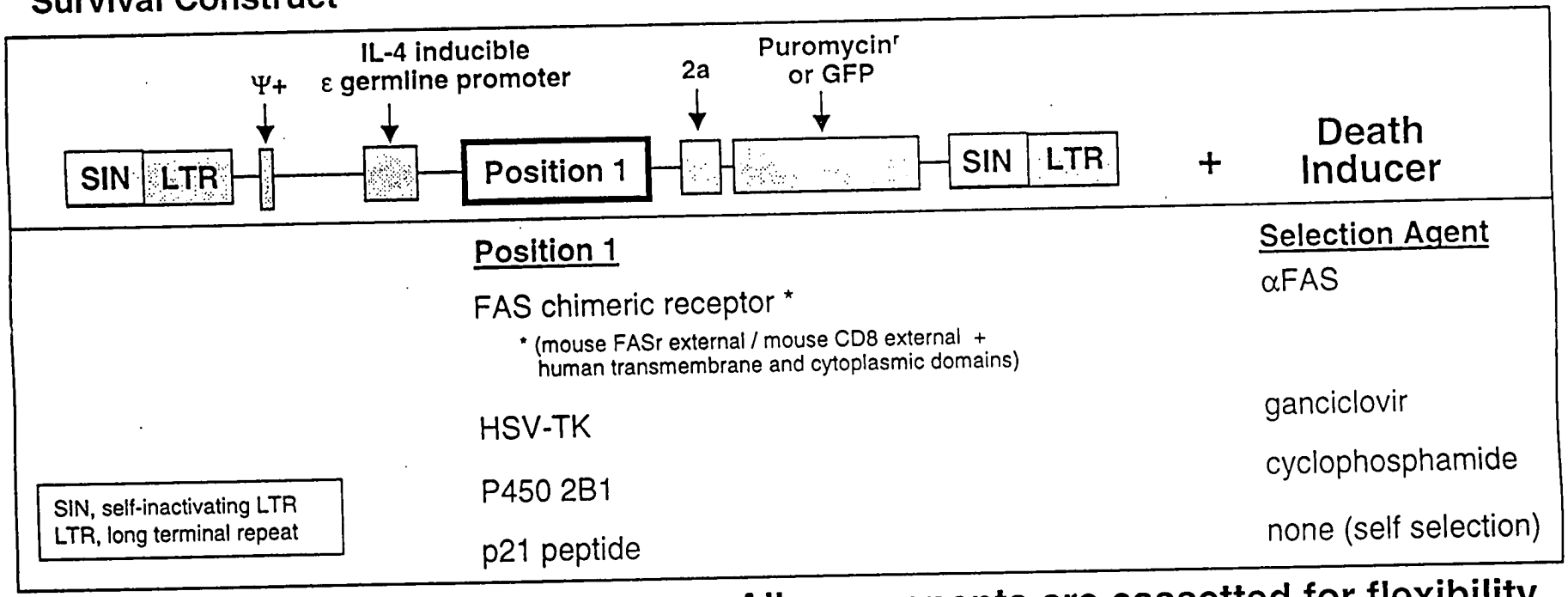
Screen for Peptide Inhibitors of the Germline ε Promoter



Survival Construct



All components are cassetted for flexibility

Appendix D

FIGURE 11A-1

1-845 CMV promoter/R/U5 5' LTR
1322 GAG ATG-ATC mutation
850-2100 extended ψ region
2146-2173 two Bstx1 peptide cloning sites
2205-2723 ECMV IRES (cloned as EcoR1/Msc1 fragment from pCITE-4a [Novagen])
2746-3465 GFP coding region
3522-4115 3' LTR
4122-6210 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATCC
CAAACTCAAATATATAAAGCATTTGACTTGTTCTATGCCCTAGTTATTAATAGTAATCAA
TTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTAA
ATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTATG
TTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACGGT
AAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACG
TCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTC
CTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGC
AGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCA
TTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTA
ACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCATGTACGGTGGGAGGTCTATATAA
GCAGAGCTCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCCAGTCCTCCGATTGACT
GAGTCGCCCGGGTACCCGTGTATCCAATAAACCCTCTTGCAGTTGCATCCGACTTGTGGT
CTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTT
CATTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCCAGGGACCACCGACCCACCACCG
GGAGGTAAGCTGGCCAGCAACTTATCTGTGTCTGTCCGATTGTCTAGTGTCTATGACTGA
TTTTATGCGCCTGCGTCGGTACTAGTTAGCTAACTAGCTCTGTATCTGGCGGACCCGTGG
TGGAACTGACGAGTTCGGAACACCCGGCCGCAACCCTGGGAGACGTCCCAGGGACTTCGG
GGGCCGTTTTTGTGGCCCGACCTGAGTCCAAAAATCCCGATCGTTTTGGACTCTTTGGTG
CACCCCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGACGAGAACCTAAAACAGTTCC
CGCCTCCGTCTGAATTTTTGCTTTCGGTTTGGGACCGAAGCCGCGCCGCGCGTCTTGTCT
GCTGCAGCATCGTTCTGTGTTGTCTCTGTCTGACTGTGTTTCTGTATTTGTCTGAAAATA
TCGGCCCGGGCCAGACTGTTACCACTCCCTTAAGTTTGACCTTAGGTCACTGGAAAGATG
TCGAGCGGATCGCTCACAACCAGTCGGTAGATGTCAAGAAGAGACGTTGGGTTACCTTCT
GCTCTGCAGAATGGCCAACCTTTAACGTCGGATGGCCGCGAGACGGCACCTTTAACCGAG
ACCTCATCACCCAGGTTAAGATCAAGGTCTTTTCACCTGGCCCGCATGGACACCCAGACC
AGGTCCCCTACATCGTGACCTGGGAAGCCTTGGCTTTTGACCCCCCTCCCTGGGTCAAGC
CCTTTGTACACCCTAAGCCTCCGCCTCCTCTTCCTCCATCCGCCCCGTCTCTCCCCCTTG
AACCTCCTCGTTCGACCCCGCCTCGATCCTCCCTTTATCCAGCCCTCACTCCTTCTCTAG
GCGCCCCCATATGGCCATATGAGATCTTATATGGGGCACCCCCGCCCCTTGTAAACTTCC
CTGACCCTGACATGACAAGAGTTACTAACAGCCCCTCTCTCCAAGCTCACTTACAGGCTC
TCTACTTAGTCCAGCACGAAGTCTGGAGACCTCTGGCGGCAGCCTACCAAGAACAACTGG
ACCGACCGGTGGTACCTCACCCTTACCGAGTCGGCGACACAGTGTGGGTCCGCCGACACC
AGACTAAGAACCTAGAACCTCGCTGGAAAGGACCTTACACAGTCCTGCTGACCACCCCCA
CCGCCCTCAAAGTAGACGGCATCGCGCTTGGATACACGCCGCCCACGTGAAGGCTGCCGA
CCCCGGGGGTGGACCATCCTCTAGACTGCCGGATCTCGAGGGATCCACCACCATGGACCC
CCATTAAATTGGAATTCCTGCAGCCCGGGGGATCCACTAGTTCTAGAGCGAATTAATTCC

FIGURE 11A-2

GGTTATTTTCCACCATATTGCCGTCTTTTGGCAATGTGAGGGCCCGGAAACCTGGCCCTG
TCTTCTTGACGAGCATTCCTAGGGGTCTTTCCCCTCTCGCCAAAGGAATGCAAGGTCTGT
TGAATGTCGTGAAGGAAGCAGTTCCTCTGGAAGCTTCTTGAAGACAAACAACGTCTGTAG
CGACCCTTTGCAGGCAGCGGAACCCCCCACCTGGCGACAGGTGCCTCTGCGGCCAAAAGC
CACGTGTATAAGATACACCTGCAAAGGCGGCACAACCCCAGTGCCACGTTGTGAGTTGGA
TAGTTGTGGAAAGAGTCAAATGGCTCTCCTCAAGCGTATTCAACAAGGGGCTGAAGGATG
CCCAGAAGGTACCCCATTGTATGGGATCTGATCTGGGGCCTCGGTGCACATGCTTTACAT
GTGTTTAGTCGAGGTTAAAAAACGTCTAGGCCCCCCGAACCACGGGGACGTGGTTTTCCT
TTGAAAAACACGATGATAATATGGGGGATCCACCGGTCGCCACCATGGTGAGCAAGGGCG
AGGAGCTGTTCACCGGGGTGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAACGGCC
ACAAGTTCAGCGTGTCCGGCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCTGA
AGTTCATCTGCACCACCGGCAAGCTGCCCGTGCCCTGGCCCACCCTCGTGACCACCCTGA
CCTACGGCGTGCAGTGCTTCAGCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCA
AGTCCGCCATGCCCGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACGACGGCA
ACTACAAGACCCGCGCCGAGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGC
TGAAGGGCATCGACTTCAAGGAGGACGGCAACATCCTGGGGCACAAGCTGGAGTACAACT
ACAACAGCCACAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATCAAGGTGAACT
TCAAGATCCGCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCAGCAGA
ACACCCCCATCGGCGACGGCCCCGTGCTGCTGCCCGACAACCACTACCTGAGCACCCAGT
CCGCCCTGAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTCCTGCTGGAGTTCGTGA
CCGCCGCCGGGATCACTCTCGGCATGGACGAGCTGTACAAGTAAAGCGGCCGCTCGACGA
TAAAATAAAAGATTTTATTTAGTCTCCAGAAAAAGGGGGGAATGAAAGACCCCACCTGTA
GGTTTGGCAAGCTAGCTTAAGTAACGCCATTTTGCAAGGCATGGAAAAATACATAACTGA
GAATAGAGAAGTTCAGATCAAGGTCAGGAACAGATGGAACAGCTGAATATGGGCCAAACA
GGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGAACAGCTG
AATATGGGCCAAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAA
CAGATGGTCCCCAGATGCGGTCCAGCCCTCAGCAGTTTCTAGAGAACCATCAGATGTTTC
CAGGGTGCCCCAAGGACCTGAAATGACCCTGTGCCTTATTTGAACTAACCAATCAGTTCG
CTTCTCGCTTCTGTTCGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGCCCACAACCCC
TCACTCGGGGCGCCAGTCCTCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAA
ACCCTCTTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGA
GTGATTGACTACCCGTCAGCGGGGGTCTTTCATTTCCGACTTGTGGTCTCGCTGCCTTGG
GAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTCACATGCAGCATGTAT
CAAAATTAATTTGGTTTTTTTTCTTAAGTATTTACATTAAATGGCCATAGTTGCATTAAT
GAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGCGCTCTTCCGCTTCCTCGCT
CACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGC
GGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGG
CCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCG
CCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGG
ACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGAC
CCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCA
TAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGT
GCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTC
CAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAG
AGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACAC
TAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGT
TGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAA
GCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGG
GTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAA
AAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTGCGCAAATCAATCTAAAG
TATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTC
AGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTAC
GATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTC
ACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGG

Express Mail No. EV 045 705 205 US

FIGURE 11A-3

TCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAG
TAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTC
ACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTAC
ATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAG
AAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTAC
TGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTG
AGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAACACGGGATAATACCGC
GCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACT
CTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTG
ATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAA
TGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTT
TCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATG
TATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTC

EDV2020-0000

FIGURE 11B-1

1-845 CMVpormoter/R/U5 5' LTR
1322 GAG ATG-ATC mutation
850-2100 extended □ region
2151-2865 GFP coding region
2866-2894 GGGSGGG linker
2895-2952 FMDV 2a cleavage sequence
2953-3004 Bstx1/Bstx1/HinD3/Hpa1/Sal1/Not1 polylinker
3052-3645 3' LTR
3652-5715 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATC
CCAAACTCAAATATATAAAGCATTTGACTTGTTCTATGCCCTAGTTATTAATAGTAATC
AATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGG
TAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACG
TATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTT
ACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTA
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GACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCG
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TCCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCA
AAATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCATGTACGGTGGGA
GGTCTATATAAGCAGAGCTCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCCAGTC
CTCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAAACCCTCTTGCAGTTGCA
TCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGT
CAGCGGGGGTCTTTCATTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCCAGGGACC
ACCGACCCACCACCGGGAGGTAAGCTGGCCAGCAACTTATCTGTGTCTGTCCGATTGTC
TAGTGTCTATGACTGATTTTATGCGCCTGCGTCGGTACTAGTTAGCTAACTAGCTCTGT
ATCTGGCGGACCCGTGGTGGAACTGACGAGTTCGGAACACCCGGCCGCAACCCTGGGAG

FIGURE 11B-2

ACGTCCCAGGGACTTCGGGGGCCGTTTTTGTGGCCCGACCTGAGTCCAAAAATCCCGAT
CGTTTTGGACTCTTTGGTGCACCCCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGA
CGAGAACCTAAAACAGTTCCCGCCTCCGTCTGAATTTTTGCTTTCGGTTTGGGACCGAA
GCCGCGCCGCGCGTCTTGTCTGCTGCAGCATCGTTCTGTGTTGTCTCTGTCTGACTGTG
TTTCTGTATTTGTCTGAAAATATCGGCCCGGGCCAGACTGTTACCACTCCCTTAAGTTT
GACCTTAGGTCACTGGAAAGATGTCGAGCGGATCGCTCACAACCAGTCGGTAGATGTCA
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CCGCGAGACGGCACCTTTAACCGAGACCTCATCACCCAGGTTAAGATCAAGGTCTTTTC
ACCTGGCCCGCATGGACACCCAGACCAGGTCCCCTACATCGTGACCTGGGAAGCCTTGG
CTTTTGACCCCCCTCCCTGGGTCAAGCCCTTTGTACACCCTAAGCCTCCGCCTCCTCTT
CCTCCATCCGCCCCGTCTCTCCCCCTTGAACCTCCTCGTTCGACCCCGCCTCGATCCTC
CCTTTATCCAGCCCTCACTCCTTCTCTAGGCGCCCCCATATGGCCATATGAGATCTTAT
ATGGGGCACCCCCGCCCCTTGTAAACTTCCCTGACCCTGACATGACAAGAGTTACTAAC
AGCCCCTCTCTCCAAGCTCACTTACAGGCTCTCTACTTAGTCCAGCACGAAGTCTGGAG
ACCTCTGGCGGCAGCCTACCAAGAACAACTGGACCGACCGGTGGTACCTCACCCTTACC
GAGTCGGCGACACAGTGTGGGTCCGCCGACACCAGACTAAGAACCTAGAACCTCGCTGG
AAAGGACCTTACACAGTCCTGCTGACCACCCCCACCGCCCTCAAAGTAGACGGCATCGC
AGCTTGGATACACGCCGCCCACGTGAAGGCTGCCGACCCCGGGGGTGGACCATCCTCTA
GACTGCCGGATCTCGAGGGATCCACCATGGTGAGCAAGGGCGAGGAGCTGTTCACCGGG
GTGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAACGGCCACAAGTTCAGCGTGTC
CGGCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCTGAAGTTCATCTGCACCA
CCGGCAAGCTGCCCGTGCCCTGGCCCACCCTCGTGACCACCCTGACCTACGGCGTGCAG
TGCTTCAGCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCAAGTCCGCCATGCC
CGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACGACGGCAACTACAAGACCC
GCGCCGAGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGCTGAAGGGCATC
GACTTCAAGGAGGACGGCAACATCCTGGGGCACAAGCTGGAGTACAACTACAACAGCCA
CAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATCAAGGTGAACTTCAAGATCC
GCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCAGCAGAACACCCCC
ATCGGCGACGGCCCCGTGCTGCTGCCCGACAACCACTACCTGAGCACCCAGTCCGCCCT
GAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTCCTGCTGGAGTTCGTGACCGCCG
CCGGGATCACTCTCGGCATGGACGAGCTGTACAAGGAATTCGGAGGTGGCAGCGGTGGC
GGTCAGCTGTTGAATTTTGACCTTCTTAAACTTGCGGGAGACGTCGAGTCCAACCCTGG
GCCCACCACCACCATGGAAGCTTCCATTAAATTGGTTAACGTCGACGCGGCCGCTCGAC
GATAAAATAAAAGATTTTATTTAGTCTCCAGAAAAAGGGGGGAATGAAAGACCCCACCT
GTAGGTTTGGCAAGCTAGCTTAAGTAACGCCATTTTGCAAGGCATGGAAAAATACATAA
CTGAGAATAGAGAAGTTCAGATCAAGGTCAGGAACAGATGGAACAGCTGAATATGGGCC
AAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGAA
CAGCTGAATATGGGCCAAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGG
CCAAGAACAGATGGTCCCCAGATGCGGTCCAGCCCTCAGCAGTTTCTAGAGAACCATCA
GATGTTTCCAGGGTGCCCCAAGGACCTGAAATGACCCTGTGCCTTATTTGAACTAACCA
ATCAGTTCGCTTCTCGCTTCTGTTCGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGC
CCACAACCCCTCACTCGGGGCGCCAGTCCTCCGATTGACTGAGTCGCCCGGGTACCCGT
GTATCCAATAAACCCTCTTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAG
GGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTTCATTTCCGACTTGTGGT
CTCGCTGCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTCA
CATGCAGCATGTATCAAAATTAATTTGGTTTTTTTTCTTAAGTATTTACATTAAATGGC
CATAGTTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGCGCT

10/5/2005 15:03:00

FIGURE 11B-3

CTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTA
TCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAA
GAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGG
CGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAG
AGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCT
CGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTT
CGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTC
GTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTT
ATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAG
CAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTG
AAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCT
GAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCG
CTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCT
CAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACG
TTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATT
AAAAATGAAGTTTGCGCAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGT
TACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCAT
AGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCC
CCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATA
AACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCAT
CCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGC
GCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTTGGTATGGCT
TCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAA
AAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGT
TATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGA
TGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCG
ACCGAGTTGCTCTTGCCCGGCGTCAACACGGGATAATACCGCGCCACATAGCAGAACTT
TAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCG
CTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTT
TACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGG
GAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGA
AGCATTTATCAGGGTTATTGTCTCATGACATTAACCTATAAAAATAGGCGT

Docket No. 2005-0205

FIGURE 11C-1

1-845 CMVpormoter/R/U5 5' LTR
1322 GAG ATG-ATC mutation
850-2100 extended [illegible] region
2146-2173 two Bstx1 peptide cloning sites
2173-2214 EoR1/Apa1/Hpa1/Not1 polylinker
2262-2855 3' LTR
2855-4901 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATCCCAAACTCAAAT
ATATAAAGCATTTGACTTGTTCTATGCCCTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAG
CCATATATGGAGTTCCGCGTTACATAACTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCG
CCCATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGG
TGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATT
GACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTTG
GCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAATGGGCGTG
GATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCAC
CAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCATGT
ACGGTGGGAGGTCTATATAAGCAGAGCTCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCCAGTCCTC
CGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAAACCCTCTTGCAGTTGCATCCGACTTGTGGTCT
CGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTTCATTTGGGGGCTC
GTCCGGGATCGGGAGACCCCTGCCCAGGGACCACCGACCCACCACCGGGAGGTAAGCTGGCCAGCAACTTA
TCTGTGTCTGTCCGATTGTCTAGTGTCTATGACTGATTTTATGCGCCTGCGTCGGTACTAGTTAGCTAACT
AGCTCTGTATCTGGCGGACCCGTGGTGGAACTGACGAGTTCGGAACACCCGGCCGCAACCCTGGGAGACGT
CCCAGGGACTTCGGGGGCCGTTTTTGTGGCCCGACCTGAGTCCAAAAATCCCGATCGTTTTGGACTCTTTG
GTGCACCCCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGACGAGAACCTAAAACAGTTCCCGCCTCCG
TCTGAATTTTTGCTTTCGGTTTGGGACCGAAGCCGCGCCGCGCGTCTTGTCTGCTGCAGCATCGTTCTGTG
TTGTCTCTGTCTGACTGTGTTTCTGTATTTGTCTGAAAATATCGGCCCGGGCCAGACTGTTACCACTCCCT
TAAGTTTGACCTTAGGTCACTGGAAAGATGTCGAGCGGATCGCTCACAACCAGTCGGTAGATGTCAAGAAG
AGACGTTGGGTTACCTTCTGCTCTGCAGAATGGCCAACCTTTAACGTCGGATGGCCGCGAGACGGCACCTT
TAACCGAGACCTCATCACCCAGGTTAAGATCAAGGTCTTTTCACCTGGCCCGCATGGACACCCAGACCAGG
TCCCCTACATCGTGACCTGGGAAGCCTTGGCTTTTGACCCCCCTCCCTGGGTCAAGCCCTTTGTACACCCT
AAGCCTCCGCCTCCTCTTCCTCCATCCGCCCCGTCTCTCCCCCTTGAACCTCCTCGTTCGACCCCGCCTCG
ATCCTCCCTTTATCCAGCCCTCACTCCTTCTCTAGGCGCCCCCATATGGCCATATGAGATCTTATATGGGG
CACCCCCGCCCCTTGTAAACTTCCCTGACCCTGACATGACAAGAGTTACTAACAGCCCCTCTCTCCAAGCT
CACTTACAGGCTCTCTACTTAGTCCAGCACGAAGTCTGGAGACCTCTGGCGGCAGCCTACCAAGAACAACT
GGACCGACCGGTGGTACCTCACCCTTACCGAGTCGGCGACACAGTGTGGGTCCGCCGACACCAGACTAAGA
ACCTAGAACCTCGCTGGAAAGGACCTTACACAGTCCTGCTGACCACCCCCACCGCCCTCAAAGTAGACGGC
ATCGCAGCTTGGATACACGCCGCCCACGTGAAGGCTGCCGACCCCGGGGGTGGACCATCCTCTAGACTGCC
GGATCTCGAGGGATCCACCACCATGGACCCCCATTAAATTGGAATTCGGGGCCCAAGCTTTGTTAACGTCG
ACGCGGCCGCCGTCGACGATAAAATAAAAGATTTTATTTAGTCTCCAGAAAAAGGGGGGAATGAAAGACCC
CACCTGTAGGTTTGGCAAGCTAGCTTAAGTAACGCCATTTTGCAAGGCATGGAAAAATACATAACTGAGAA
TAGAGAAGTTCAGATCAAGGTCAGGAACAGATGGAACAGCTGAATATGGGCCAAACAGGATATCTGTGGTA
AGCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGAACAGCTGAATATGGGCCAAACAGGATATCTGT
GGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGTCCCCAGATGCGGTCCAGCCCTCAGCAGT
TTCTAGAGAACCATCAGATGTTTCCAGGGTGCCCCAAGGACCTGAAATGACCCTGTGCCTTATTTGAACTA
ACCAATCAGTTCGCTTCTCGCTTCTGTTCGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGCCCACAACC
CCTCACTCGGGGCGCCAGTCCTCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAAACCCTCTTG

Exhibit No. 1003 Page 0

FIGURE 11C-2

CAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGC
GGGGGTCTTTCATTTCCGACTTGTGGTCTCGCTGCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGT
CAGCGGGGGTCTTCACATGCAGCATGTATCAAAATTAATTTGGTTTTTTTTCTTAAGTATTTACATTAAAT
GGCCATAGTTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGCGCTCTTCCGCTT
CCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTA
ATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAG
GAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATC
GACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCC
CTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGT
GGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTG
TGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTA
AGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGC
TACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGC
TGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGT
GGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTC
TACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGA
TCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTGCGCAAATCAATCTAAAGTATATATGAGTAAACT
TGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCAT
AGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAA
TGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAG
CGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAG
TAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGT
TTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAA
AAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGT
TATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACT
CAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAACACGGGATAAT
ACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAG
GATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTA
CTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACA
CGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCAT
GACATTAACCTATAAAAATAGGCGT

2020-0209-2

FIG 12A

(1) C12ScFas Survival construct

C12ScFas: epsilon-cFas(CD95)-Ires-Hygro-BGH PolyA put into C12s vector backwards so that no leaky transcription happens through the cmv promoter. .

atcacgaggccctttcgtcttcaagaacagctttgctcttaggagtttcctaatacatcccaaactcaaatatataaagc
atttgacttgttctatgccctagttattaatagtaatcaattacggggtcattagttcatagcccatatatggagttccg
cgttacataacttacggtaaatggcccgcctggctgaccgcccaacgacccccgcccattgacgtcaataatgacgtatg
ttcccatagtaacgccaatagggactttccattgacgtcaatgggtggagtatttacggtaaactgcccacttggcagta
catcaagtgtatcatatgccaagtacgcccccctattgacgtcaatgacggtaaatggcccgcctggcattatgcccagta
catgaccttatgggactttcctacttggcagtacatctacgtattagtcatcgctattaccatggtgatgcggttttggc
agtacatcaatgggcgtggatagcggtttgactcacggggatttccaagtctccaccccattgacgtcaatgggagtttg
ttttggcaccaaaatcaacgggactttccaaaatgtcgtaacaactccgccccattgacgcaaatgggcggtaggcatgt
acggtgggaggtctatataagcagagctcaataaaagagcccacaacccctcactcggggcgccagtcctccgattgact
gagtcgcccgggtacccgtgtatccaataaaccctcttgcagttgcatccgacttgtggtctcgctgttccttgggaggg
tctcctctgagtgattgactacccgtcagcgggggtctttcatttgggggctcgtccgggatcgggagacccctgcccag
ggaccaccgacccaccaccgggaggtaagctggccagcaacttatctgtgtctgtccgattgtctagtgtctatgactga
ttttatgcgcctgcgtcggtactagttagctaactagctctgtatctggcggacccgtggtggaactgacgagttcggaa
cacccggccgcaaccctgggagacgtcccagggacttcgggggccgtttttgtggcccgacctgagtccaaaaatcccga
tcgttttggactctttggtgcaccccccttagaggagggatatgtggttctggtaggagacgagaacctaaaacagttcc
cgcctccgtctgaatttttgctttcggtttgggaccgaagccgcgccgcgcgtcttgtctgctgcagcatcgttctgtgt
tgtctctgtctgactgtgtttctgtatttgtctgaaaatatgggcccgggccagactgttaccactcccttaagtttgac
cttaggtcactggaaagatgtcgagcggatcgctcacaaccagtcggtagatgtcaagaagagacgttgggttaccttct
gctctgcagaatggccaacctttaacgtcggatggccgcgagacggcacctttaaccgagacctcatcacccaggttaag
atcaaggtcttttcacctggcccgcatggacacccagaccaggtcccctacatcgtgacctgggaagccttggcttttga
ccccctccctgggtcaagccctttgtacaccctaagcctccgcctcctcttcctccatccgccccgtctctcccccttg
aacctcctcgttcgaccccgcctcgatcctccctttatccagccctcactccttctctaggcgccccatatggccatat
gagatcttatatggggcacccccgccccttgtaaacttccctgaccctgacatgacaagagttactaacagcccctctct
ccaagctcacttacaggctctctacttagtccagcacgaagtctggagacctctggcggcagcctaccaagaacaactgg
accgaccggtggtacctcaccctaccgagtcggcgacacagtgtgggtccgccgacaccagactaagaacctagaacct
cgctggaaaggaccttacacagtcctgctgaccacccccaccgccctcaaagtagacggcatcgcagcttggatacacgc
cgcccacgtgaaggctgccgaccccgggggtggaccatcctctagactgccGGATCTCGAGGGATCCTCCCCAGCATGCC

TGCTATTGTCTTCCCAATCCTCCCCCTTGCTGTCCTGCCCCACCCCACCCCCCAGAATAGAATGACACCTACTCAGACAA

TGCGATGCAATTTCCTCATTTTATTAGGAAAGGACAGTGGGAGTGGCACCTTCCAGGGTCAAGGAAGGCACGGGGGAGGG

GCAAACAACAGATGGCTGGCAACTAGAAGGCACAGTCGAGGtCTAGCTTGCCAAACCTACAGGTGGGGTCTTTCATTCCC

CCCTTTTTCTGGAGACTAAATAAAATCTTTTATTTTatcgatagatcccggtcggcatctactctattcctttgccctcg
gacgagtgctggggcgtcggtttccactatcggcgagtacttctacacagccatcggtccagacggccgcgcttctgcgg
gcgatttgtgtacgcccgacagtcccggctccggatcggacgattgcgtcgcatcgaccctgcgcccaagctgcatcatc
gaaattgccgtcaaccaagctctgatagagttggtcaagaccaatgcggagcatatacgcccggagccgcggcgatcctg
caagctccggatgcctccgctcgaagtagcgcgtctgctgctccatacaagccaaccacggcctccagaagaagatgttg
gcgacctcgtattgggaatccccgaacatcgcctcgctccagtcaatgaccgctgttatgcggccattgtccgtcaggac
attgttggagccgaaatccgcgtgcacgaggtgccggacttcggggcagtcctcggcccaaagcatcagctcatcgagag
cctgcgcgacggacgcactgacggtgtcgtccatcacagtttgccagtgatacacatggggatcagcaatcgcgcatatg
aaatcacgccatgtagtgtattgaccgattccttgcggtccgaatgggccgaacccgctcgtctggctaagatcggccgc
agcgatcgcatccatggcctccgcgaccggctgcagaacagcgggcagttcggtttcaggcaggtcttgcaacgtgacac
cctgtgcacggcgggagatgcaataggtcaggctctcgctaaattccccaatgtcaagcacttccggaatcgggagcgcg
gccgatgcaaagtgccgataaacataacgatctttgtagaaaccatcggcgcagctatttacccgcaggacatatccacg
ccctcctacatcgaagctgaaagcacgagattcttcgccctccgagagctgcatcaggtcggagacgctgtcgaacttttt
cgatcagaaacttctcgacagacgtcgcggtgagttcaggctttttcatggtattatcatcgtgtttttcaaaggaaaac
cacgtccccgtggttcgggggcctagacgtttttttaacctcgactaaacacatgtaaagcatgtgcaccgaggccccag
atcagatcccatacaatggggtaccttctgggcatccttcagccccttgttgaatacgcttgaggagagccatttgactc
tttccacaactatccaactcacaacgtggcactggggttgtgccgcctttgcaggtgtatcttatacacgtggcttttgg
ccgcagaggcacctgtcgccaggtgggggttccgctgcctgcaaagggtcgctacagacgttgtttgtcttcaagaagc
ttCCAGAGGAACTGCTTCCTTCACGACATTCAACAGACCTTGCATTCCTTTGGCGAGAGGGGAAAGACCCctagactaga

ccaagctttggatttcatttctgaagtttgaattttctgagtcactagtaatgtccttgaggatgatagtctgaattttc
tctgcaagagtacaaagattggctttttttgagatctttaatcaatgtgtcatacgcttctttctttccatgaagttgatg
ccaattacgaagcagttgaacttctgttctgctgtgtcttggacattgtcattcttgatctcatctattttggcttcat
tgacaccattctttcgaacaaagcctttaacttgacttagtgtcatgactccagcaatagtggtgatatatttactcaag
tcaacatcagataaatttattgccactgtttcaggatttaaggttggagattcatgagaaccttggttttcctttctgtg
ctttctgcatgttttctgtacttcctttctcttcacccaaacaattagtggaattggcaaaagaagaagacaaagccacc
ccaaccggTTTCTGGGACTTTGTTTCCTGCAGTTTGTATTGCTGGTTGCTGTGCATGGCTCAAGGGTTCCATGTTCACAC

GAGGCGCAGCGAACACAGTGTTCACAGCCAGGAGAATCGCAGTAGAAGTCTGGTTTGCACTTGCACTTGGTATTCTGGGT

CAGGGTGCAGTTTGTTTCCACTTCTAAACCATGCTCTTCATCGCAGAGTGTGCATCTTCTGCATTTATCAGCATAATGGT

TCTTGTCCATGTACTCCTTCCCTTCTGTGCATGGGGCACAGGTTGGTGTACCCCCATTCATTTTGCAGTCCTCAACTTTT

Exhibit 2003

FIG 12B

TTTTTACCAGGTTGGCATGGTTGACAGCAAAATGGGCCTCCTTGATATAATCCTTCTGAGCAGTTTTTATCAGTTTCATG

AACCCGCCTCCTCAGCTTTAAACTCTCGGAGATGCTATTAGTACCTTGAGTATGAACTCTTAACTGTGAGCCAGCAAGCA

CCAGAGGCAGGACAGCCCAGATCCACACCATgGTGGCTTTACCAACAGTACCGGAATGCCAAGCTTGCGGCCGCTTAAGA

GCTGTAATTGAACCTGGGAGTGGACACCTGTGGAGAGAAAGGCAAAGTGGATGTCAGTAAGACCAATAGGTGCCTATCAG

AAACGCAAGAGTCTTCTCTGTCTCGACAAGCCCAGTTTCTATTGGTCTCCTTAAACCTGTCTTGTAACCTTGATACTTAC

CTGCCCAGTGCCTCACGACCAACTTctgcaggaattcctggacagctcccagatgatcagtaaccgtggttgttatttct
gtgccgggcagtggagcctgggtaggggagctctgcctcagtgctttcagctaaaaatggggtgggaaccccCaggagg
cccgggccgccctggaagttccctttctctctgttcttgggaagtcgattgagcaacagcgggggtcaggtgaggctcc
ttcactaccgatgcacaccgagtgctGggggaggttctcttctctctcaggcccaacCccagggcccctgcctaggtccc
ggactctCactcttgacgcatgcgtggcttggtggtcccagtcagcaaacttggggtcccgttgcctgggaaagggagag
ggtactgggcatcgacgcctctgcttccacgaaagccttgtgaagaaaggatgggggcgcttttgtgcaggagaatgagg
cgcactgaggtgaactggccctcggggGcgcgtgtcccagatgtgtgtgcagggcctcctgatggccgcagccctcgtcc
ctgtgacccgcttggagctggcaccctgagtggtggcctcacCTTGTACTCACTCCCAGGTCACTGTCCtcgacGCGGCC

GCTCGAcgatAAAATAAAAGATTTTATTTAGTCTCCAGAAAAAGGGGGGAATGAAAGACCCCACCTGTAGGTTTGGCAAg

ctagcTTAAGTAACCCATTTTGCAAGGCATGGAAAAATACATAACTGAGAATAGAGAAGTTCAGATCAAGGTCGGAACAG

ATGGAACAGGCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCCAGTCCTCCGATTGACTGAGTCGCCCGGGTACCCG

TGTATCCAATAAACCCTCTTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGA

CTACCCGTCAGCGGGGGTCTTTCAcatgcaGCATGTATCAAAATTAATTTGGTTTTTTTTCTTAAGTATTTACATTAAAT

GGCCATagtttcGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAG

CCGGAAGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCT

TTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCG

CTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGG

TAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGT

AAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAG

GTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCC

TGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTC

AGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGG

TAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAG

CGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATC

TGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGG

TGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGT

CTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTT

TTAAATTAAAAATGAAGTTTGCGCAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAAT

CAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGA

TACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCA

ATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTG

CCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCAC

GCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAA

AAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGC

Docket No.: 2003-0135

FIG 12C

ACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGagtactcaaccaagtcattctgag

aatagtgtatgcggcgaccgagttgctcttgcccggcgtcaacacgggataataccgcgccacatagcagaactttaaaa
gtgctcatcattggaaaacgttcttcggggcgaaaactctcaaggatcttaccgctgttgagatccagttcgatgtaacc
cactcgtgcacccaactgatcttcagcatcttttactttcaccagcgtttctgggtgagcaaaaacaggaaggcaaaatg
ccgcaaaaaagggaataagggcgacacggaaatgttgaatactcatactcttcctttttcaatattattgaagcatttat
cagggttattgtctcatgacattaacctataaaaataggcgt

Docket No. 2002-0209

FIG 13A

(2) Ahhhh: Survival construct

2.) Ahhhh: epsilon-cFas' (CD8 or mLyt2)-Ires-Hygro-BGHpolyA also in C12s backwards

atcacgaggccctttcgtcttcaagaacagctttgctcttaggagtttgctaatacatcccaaactcaaatatataaagc
atttgacttgttctatgccctagttattaatagtaatcaattacggggtcattagttcatagcccatatatggagttccg
cgttacataacttacggtaaatggcccgcctggctgaccgcccaacgacccccgcccattgacgtcaataatgacgtatg
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catcaagtgtatcatatgccaagtacgccccctattgacgtcaatgacggtaaatggcccgcctggcattatgcccagta
catgaccttatgggactttcctacttggcagtacatctacgtattagtcatcgctattaccatggtgatgcggttttggc
agtacatcaatgggcgtggatagcggtttgactcacggggatttccaagtctccaccccattgacgtcaatgggagtttg
ttttggcaccaaaatcaacgggactttccaaaatgtcgtaacaactccgccccattgacgcaaatgggcggtaggcatgt
acggtgggaggtctatataagcagagctcaataaaagagcccacaacccctcactcggggcgccagtcctccgattgact
gagtcgcccgggtacccgtgtatccaataaaccctcttgcagttgcatccgacttgtggtctcgctgttccttgggaggg
tctcctctgagtgattgactacccgtcagcgggggtctttcatttgggggctcgtccgggatcgggagacccctgcccag
ggaccaccgacccaccaccgggaggtaagctggccagcaacttatctgtgtctgtccgattgtctagtgtctatgactga
ttttatgcgcctgcgtcggtactagttagctaactagctctgtatctggcggacccgtggtggaactgacgagttcggaa
cacccggccgcaaccctgggagacgtcccagggacttcgggggccgtttttgtggcccgacctgagtccaaaaatcccga
tcgttttggactctttggtgcacccccttagaggagggatatgtggttctggtaggagacgagaacctaaaacagttcc
cgcctccgtctgaatttttgctttcggtttgggaccgaagccgcgccgcgcgtcttgtctgctgcagcatcgttctgtgt
tgtctctgtctgactgtgtttctgtatttgtctgaaaatatgggcccgggccagactgttaccactcccttaagtttgac
cttaggtcactggaaagatgtcgagcggatcgctcacaaccagtcggtagatgtcaagaagagacgttgggttaccttct
gctctgcagaatggccaacctttaacgtcggatggccgcgagacggcacctttaaccgagacctcatcacccaggttaag
atcaaggtcttttcacctggcccgcatggacacccagaccaggtcccctacatcgtgacctgggaagccttggcttttga
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aacctcctcgttcgaccccgcctcgatcctccctttatccagccctcactccttctctaggcgcccccatatggccatat
gagatcttatatggggcaccccgcccccttgtaaacttccctgaccctgacatgacaagagttactaacagcccctctct
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accgaccggtggtacctcacccttaccgagtcggcgacacagtgtgggtccgccgacaccagactaagaacctagaacct
cgctggaaaggaccttacacagtcctgctgaccacccccaccgccctcaaagtagacggcatcgcagcttggatacacgc
cgcccacgtgaaggctgccgaccccgggggtggaccatcctctagactgccGGATCTCGAGGGATCCTCCCCAGCATGCC

TGCTATTGTCTTCCCAATCCTCCCCCTTGCTGTCCTGCCCCACCCCACCCCCCAGAATAGAATGACACCTACTCAGACAA

TGCGATGCAATTTCCTCATTTTATTAGGAAAGGACAGTGGGAGTGGCACCTTCCAGGGTCAAGGAAGGCACGGGGGAGGG

GCAAACAACAGATGGCTGGCAACTAGAAGGCACAGTCGAGGtCTAGCTTGCCAAACCTACAGGTGGGGTCTTTCATTCCC

CCCTTTTTCTGGAGACTAAATAAAATCTTTTATTTTatcgatagatcccggtcggcatctactctattcctttgccctcg
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gcgatttgtgtacgcccgacagtcccggctccggatcggacgattgcgtcgcatcgaccctgcgcccaagctgcatcatc
gaaattgccgtcaaccaagctctgatagagttggtcaagaccaatgcggagcatatacgcccggagccgcggcgatcctg
caagctccggatgcctccgctcgaagtagcgcgtctgctgctccatacaagccaaccacggcctccagaagaagatgttg
gcgacctcgtattgggaatccccgaacatcgcctcgctccagtcaatgaccgctgttatgcggccattgtccgtcaggac
attgttggagccgaaatccgcgtgcacgaggtgccggacttcggggcagtcctcggcccaaagcatcagctcatcgagag
cctgcgcgacggacgcactgacggtgtcgtccatcacagtttgccagtgatacacatggggatcagcaatcgcgcatatg
aaatcacgccatgtagtgtattgaccgattccttgcggtccgaatgggccgaacccgctcgtctggctaagatcggccgc
agcgatcgcatccatggcctccgcgaccggctgcagaacagcgggcagttcggtttcaggcaggtcttgcaacgtgacac
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gccgatgcaaagtgccgataaacataacgatctttgtagaaaccatcggcgcagctatttacccgcaggacatatccacg
ccctcctacatcgaagctgaaagcacgagattcttcgccctccgagagctgcatcaggtcggagacgctgtcgaacttttt
cgatcagaaacttctcgacagacgtcgcggtgagttcaggctttttcatggtattatcatcgtgtttttcaaaggaaaac
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atcagatcccatacaatggggtaccttctgggcatccttcagccccttgttgaatacgcttgaggagagccatttgactc
tttccacaactatccaactcacaacgtggcactggggttgtgccgcctttgcaggtgtatcttatacacgtggcttttgg
ccgcagaggcacctgtcgccaggtgggggttccgctgcctgcaaagggtcgctacagacgttgtttgtcttcaagaagc
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ccaagctttggatttcatttctgaagtttgaattttctgagtcactagtaatgtccttgaggatgatagtctgaattttc
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ccaattacgaagcagttgaacttttctgttctgctgtgtcttggacattgtcattcttgatctcatctattttggcttcat
tgacaccattctttcgaacaaagcctttaacttgacttagtgtcatgactccagcaatagtggtgatatatttactcaag

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Fig- 13B

tcaacatcagataaatttattgccactgtttcaggatttaaggttggagattcatgagaaccttggttttcctttctgtg
ctttctgcatgttttctgtacttcctttctcttcacccaaacaattagtggaattggcaaaagaagaagacaaagccacc
ccaaccggtttccggtccccttcactgagccacggggccgacaatcttctggtctctggggctgagatgtcccggtaggg
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GAGTGGACACCTGTGGAGAGAAAGGCAAAGTGGATGTCAGTAAGACCAATAGGTGCCTATCAGAAACGCAAGAGTCTTCT

CTGTCTCGACAAGCCCAGTTTCTATTGGTCTCCTTAAACCTGTCTTGTAACCTTGATACTTACCTGCCCAGTGCCTCACG

ACCAACTTctgcaggaattcctggacagctcccagatgatcagtaaccgtggttgttatttctgtgccgggcagtggagc
ctgggtagggggagctctgcctcagtgctttcagctaaaaatggggtgggaaccccCaggaggcccgggccgccctggaa
gttccctttctctctgttcttgggaagtcgattgagcaacagcgggggtcaggtgaggctccttcactaccgatgcaca
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gccctcggggGcgcgtgtcccagatgtgtgtgcagggcctcctgatggccgcagccctcgtccctgtgacccgcttggag
ctggcaccctgagtggtggcctcacCTTGTACTCACTCCCAGGTCACTGTCCtcgacGCGGCCGCTCGAcgatAAAATAA

AAGATTTTATTTAGTCTCCAGAAAAAGGGGGGAATGAAAGACCCCACCTGTAGGTTTGGCAAgctagcTTAAGTAACCCA

TTTTGCAAGGCATGGAAAAATACATAACTGAGAATAGAGAAGTTCAGATCAAGGTCGGAACAGATGGAACAGGCAATAAA

AGAGCCCACAACCCCTCACTCGGGGCGCCAGTCCTCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAAACCCT

CTTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGG

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CATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGT

AAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCT

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TTTGCGCAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCT

CAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCA

TCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGG

AAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAA

GTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTTGGTATG

Fig. 13B

FIG 13C

GCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTT

CGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTA

CTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGagtactcaaccaagtcattctgagaatagtgtatgcggcga

ccgagttgctcttgcccggcgtcaacacgggataataccgcgccacatagcagaactttaaaagtgctcatcattggaaa
acgttcttcggggcgaaaactctcaaggatcttaccgctgttgagatccagttcgatgtaacccactcgtgcacccaact
gatcttcagcatcttttactttcaccagcgtttctgggtgagcaaaaacaggaaggcaaaatgccgcaaaaaagggaata
agggcgacacggaaatgttgaatactcatactcttccttttcaatattattgaagcatttatcagggttattgtctcat
gacattaacctataaaaataggcgt

Replacement Sheet